BB

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: 0 087 228 A1

(12) EUROPEAN PATENT APPLICATION

(21) Application number: 83300517.6

(22) Date of filing: 02.02.83

(51) Int. Cl.³: B 01 D 13/04

(30) Priority: 05.02.82 US 346118

(43) Date of publication of application: 31.08.83 Bulletin 83/35

(84) Designated Contracting States: BE DE IT NL SE

(71) Applicant: PALL CORPORATION
30 Sea Cliff Avenue
Glen Cove New York 11542(US)

(72) Inventor: Gsell, Thomas Charles
9 Grace Lane
Levittown New York 11756(US)

(72) Inventor: Joffee, Irving Brian
19 Clearview Street
Huntington New York 11743(US)

(72) Inventor: Degen, John Peter
24 Glades Way
Huntington New York 11743(US)

(74) Representative: Corin, Christopher John et al,
Mathisen Macara & Co. Lyon House Lyon Road
Harrow Middx. HA1 2ET(GB)

(54) Polyamide membrane with controlled surface properties.

(57) Surface modified, skinless, hydrophilic, microporous, polyamide membranes with controlled surface properties are prepared by the steps of preparing a casting solution comprised of (A) a casting resin system comprised of (a) an alcohol-insoluble polyamide resin, and (b) a water-soluble membrane surface modifying polymer having functional polar groups and a molecular weight of 10,000 or greater, and (B) a solvent system in which the casting resin system is soluble; inducing nucleation of the casting solution by controlled addition of a non-solvent for the casting resin system under controlled conditions to obtain a visible precipitate of casting resin system particles, thereby forming a casting composition; spreading the casting composition on a substrate to form a thin film; contacting and diluting the film of the casting composition with a liquid non-solvent system for the casting resin system, thereby precipitating the casting resin system from the casting composition in the form of a thin, skinless, hydrophilic, surface modified, microporous, polyamide membrane; and washing and drying the membrane. The membranes of this invention are characterized by having fine pore ratings, the surfaces properties thereof being substantially controlled by functional polar groups of a membrane surface modifying polymer and having the capability, through the functional polar groups of the modifying polymer, of reacting or interacting with particulates and/or nonparticulates in a fluid. Membranes of this invention are useful in removing metal species from aqueous streams and in immobilizing enzymes. Membranes of this invention also have enhanced filtration efficiency over a broad pH range with very fine contaminants, particularly very fine positively charged particles, such as asbestos.

EP 0 087 228 A1

Croydon Printing Company Ltd.

POLYAMIDE MEMBRANE WITH CONTROLLED SURFACE PROPERTIES

The present invention relates to microporous membranes.

Microporous membranes have been recognized as useful for filtering fine particles from gas and liquid media. United States patent specification 4,340,479 discloses a process for manufacturing microporous polyamide membranes with certain desirable filtration characteristics. Such membranes are hydrophilic, have narrow pore size distributions and pore ratings as fine as 0.04 micrometer. For many filtering requirements, those membranes perform very effectively.

The effectiveness of a filter membrane in a given application is a reflection of the nature of the filter membrane and the material being filtered. A filter membrane can achieve fluid clarification by different mechanisms. Particulate material can be removed through mechanical sieving wherein all particles larger than the pore diameter of the filter membrane are removed from the fluid. A filter may also remove suspended particulate material by adsorption onto the filter

membrane surfaces. Removal of particulate material by this mechanism is controlled by the surface characteristics of (1) the suspended particulate material and (2) the filter membrane.

Colloid stability theory can be used to predict the interactions of electrostatically charged particles and surfaces. If the charges of suspended particle and the filter membrane surface are of like sign and with zeta potentials of greater than about 20mV, mutual repulsive forces will be sufficiently strong to prevent capture by adsorption. If the zeta potentials of the suspended particles and the filter membrane surface are small, or of opposite sign, particles will tend to adhere to the filter membrane surfaces. By careful control of the zeta potential of the filter material, selective particulate removal can be achieved.

There are many industrial processes in which it is desired to remove larger particles from suspensions of costly smaller particles, e.g. catalysts and colloidal drugs. In such applications, it is extremely undesirable if the filter intended to act as a sieve for the larger particles removes a portion of the costly smaller particles fraction by adsorption. There are also applications, such as the filtration of beverages,

where flavour components and/or dyes are present in colloidal form. In these cases, too, removal of these components by adsorption onto the filter membrane is undesirable. Because most suspensions of particles encountered in industrial practice have a negative zeta potential, such unwanted adsorptive removal can be minimized if a negative charge can be imparted to the filtering medium.

The unusual zeta potential versus pH profile of the membranes of U.S. Patent 4,340,479 is believed to result from the positioning of a high concentration of the amine and carboxylic acid end groups of the polyamide at the exposed surfaces of the membrane. That profile, strongly negative at pHs above 6.5, approaches zero and then becomes positive in acidic media. Accordingly, the membranes of U.S. Patent 4,340,479 have the ability to remove small negatively charged particles in acidic media by adsorption. Conversely, these membranes have limited capability to remove positively charged particles in acidic media.

By modifying the surface characteristics of the hydrophilic membranes disclosed in U.S. Patent Specification 4,340,479 to, for instance, provide a negative zeta potential over the acidic range, the

spectrum of uses for these materials in filtration would be substantially expanded.

In addition to purification by particle removal, certain of the modified membranes of this invention can simultaneously purify liquids by removal of dissolved metallic contaminants through complex formation by interaction with the metal species. The mechanisms by which this occurs are varied. Removal may occur by an ion exchange mechanism wherein a membrane modified to have a predominance of anionic groups at the membrane surfaces may behave as a cation exchange resin and trap the dissolved metal species, most of which are present as cations in aqueous solution.

Alternatively, dissolved metals may be removed from solution by a mechanism wherein the metal is bound as a stable complex or coordination compound with chemical functional groups present at the surfaces of the modified membrane. This mechanism is very useful in the removal or recovery of zero-valent metal complexes, such as those used as industrial catalysts and of negatively charged complexes, such as those found in plating baths. These two types of complexes, in which costly metals are frequently found, are not removed from solution by a cation-exchanging material.

Thus, by modifying the surface characteristics of the hydrophilic membranes disclosed in U.S. Patent specification 4,340,479 to, for instance, provide a surface with which dissolved metals would be able to react chemically, the spectrum of uses for these materials in filtration would be further expanded.

The existence of interactions between certain biological materials and other natural or synthetic materials is also well known to those skilled in the art. These interactions are used routinely in the purification of biological and biochemical preparations. One example of this is the widespread technique of affinity chromatography which is described in "Theory and Practice in Affinity Chromatography", P. V. Sundaram and F. Eckstein, Academic Press, New York, 1978. In affinity chromatography, convenient physical supports are chemically modified with substances with which various biological materials have a strong positive interaction. The use of these modified supports in a chromatographic process has enabled the separation of complex biochemical mixtures into their components. Materials which have been isolated in this manner include proteins, pyrogens and immune factors, all of which are useful products to the pharmaceutical and

biological industries. Commercial purification of such materials by means of affinity chromatography would be a very expensive operation. However, by modifying the surface characteristics of the hydrophilic membranes disclosed in U.S. Patent Specification 4,340,479 to, for instance, enable chemical modification of the membrane and thereby provide a strong affinity between certain biological materials and the membrane, the cost of such purification could be substantially reduced and the spectrum of uses of these membranes in filtration processes would again be substantially expanded.

Another technical area in which the membranes of this invention can be used is in the immobilization of enzymes. Enzymes can be chemically bound to many solid surfaces by a variety of methods known to those skilled in the art. Such methods are described in "The Proteins", J. Porath and T. Kristiansen, H. Neurath, Editor in 3rd Edition, Academic Press, 1975. Immobilized enzymes on various solid supports are presently being used in industrial operations, including food processing and preparation of pharmaceuticals. As biotechnology progresses it is expected that the use of immobilized enzymes will become even more widespread. The surface modified, microporous membranes of this invention, when used as supports for immobilized

enzymes, serve not only as a means for exposing the enzyme to the substrate, but also as a convenient means of separating the enzyme from the product, as well as a means for the simultaneous removal of unwanted particulate contaminants, such as cell debris, which is a frequent by-product in commercial enzyme preparations.

Processes in accordance with the present invention provide microporous membranes with fine pore ratings and narrow pore size distributions. Such membranes have pore surfaces bearing selected functional polar groups, providing unique and highly desirable properties enabling them to react or interact in a controlled manner with particulate matter in a fluid, non-particulate matter in a fluid, or both. This controlled reaction or interaction between the membrane and one or more of the components of the fluid make filter membranes in accordance with this invention useful in the purification of beverages, chemical process streams, and waste streams. They also can be chemically modified after formation as required for use in pharmaceutical and biological preparations.

According to the present invention there is provided a process for preparing a surface modified, skinless, hydrophilic, microporous, alcohol-insoluble polyamide

membrane with controlled pore surface properties, capable of reacting or interacting in a controlled manner with (a) particulate matter in a fluid, (b) non-particulate matter in a fluid, or (c) both (a) and (b) and that is readily wetted by water, which process comprises:

(1) preparing a casting solution comprising (A) a casting resin system including (a) an alcohol-insoluble polyamide resin having a ratio CH_2 to amide NHCO groups within the range of from 5:1 to 7:1, and (b) a water-soluble, membrane surface modifying polymer having functional polar groups and a molecular weight of 10,000 or greater, and (B) a solvent system in which said casting resin system is soluble;

(2) inducing nucleation of said casting solution by controlled addition of non-solvent for said casting resin system under controlled conditions of concentration, temperature, addition rate and degree of agitation to obtain a visible precipitate of casting resin system particles, thereby forming a casting composition;

(3) spreading said casting composition on a substrate to form a thin film thereof on the substrate;

(4) contacting and diluting the film of said casting composition with a liquid non-solvent system for said casting resin system comprising a mixture of

solvent and non-solvent liquids, thereby precipitating said casting resin system from said casting composition in the form of a thin, skinless, hydrophilic, surface modified, microporous, polyamide membrane with controlled pore surface properties;

(5) washing said membrane to remove solvent; and

(6) drying said membrane.

Preferably the casting composition is filtered to remove visible precipitated particles and the membrane is washed to remove solvent prior to the final drying of the membrane.

Surface modified, alcohol-insoluble polyamide membranes in accordance with this invention have the unusual property of being hydrophilic, i.e., they are readily wetted by water, typically being wetted through in 3 seconds or less, preferably 1 second or less, when immersed in water (see U.S. Patent Specification 4,340,479), have pore sizes (also referred to as pore ratings or pore diameters) of from about 0.04 to about 10 micrometers or more, preferably 0.1 to 5 micrometers, have, in certain instances, modified zeta potentials in acidic media, have filtration efficiencies ranging from molecular dimensions (pyrogens) to particulates larger than the pore sizes and, accordingly, are highly

desirable as filter media, particularly for producing bacterially sterile filtrates. As a result of the ability to control the surface properties of the membranes in accordance with this invention, they are also useful to remove undesired dissolved material or to concentrate desired dissolved material and to serve as supports for the immobilization of enzymes and in processing biological and biochemical preparations.

The membrane surface modifying polymers or resins useful in preparing the membranes are water-soluble polymers capable of reacting or interacting with (a) particulate matter in a fluid, (b) non-particulate matter in a fluid, or (c) both (a) and (b). They have molecular weights of 10,000 or greater, preferably 20,000 or greater. A preferred range of molecular weights is from 25,000 to 150,000. Preferred surface modifying polymers within this class are the polyethyleneimines, poly (vinyl alcohol), carboxyl-containing compositions, such as polymers of acrylic acid, and sulfonic-containing compositions, such as a homopolymer of styrene sulfonic acid.

The subject invention is directed to membranes with controlled pore surface properties, capable of reacting or interacting with (a) particulate matter in fluid, (b)

non-particulate matter in fluid, or (c) both (a) and (b), and a process for preparing these membranes by the steps of (1) preparing a casting solution comprised of (A) a resin casting system comprised of (a) an alcohol-insoluble polyamide resin having a ratio of CH_2:NHCO of methylene CH_2 to amide NHCO groups within the range of from about 5:12 to about 7:1 and (b) a membrane surface modifying polymer having functional polar groups and a molecular weight of 10,000 or greater; and (B) a solvent system in which the casting resin system is soluble; (2) inducing nucleation of the casting solution by controlled addition of a nonsolvent for the casting resin systems under controlled conditions of concentration, temperature, addition rate and degree of agitation to obtain a visible precipitate of casting resin system particles which may or may not thereafter partially or completely redissolve, thereby forming a casting composition; (3) preferably filtering the casting composition to remove visible precipitated particles; (4) spreading the casting composition on a substrate to form a thin film thereof on the substrate; (5) contacting and diluting the film of casting composition with a liquid nonsolvent system comprised of a mixture of solvent and non-solvent liquids and containing a substantial proportion of the solvent liquid but less than the proportion in the casting

solution, thereby precipitating the casting resin system from the casting composition in the form of a thin, skinless, hydrophilic, surface modified, microporous membrane; (6) washing the membrane to remove solvent; and (7) drying the membrane.

The membranes disclosed in U.S Patent Specification 4,340,479 are prepared from alcohol-insoluble polyamide resins having a methylene to amide ratio in the range of 5:1 to 7:1, as are the surface modified membranes in accordance with this invention. Members of this group include copolymers of hexamethylene diamine and adipic acid (nylon 66), copolymers of hexamethylene diamine and sebacic acid (nylon 610) and homopolymers of poly-e-caprolactam (nylon 6). The preferred member of the group is nylon 66.

In the process for manufacturing the membranes of U.S. Patent Specification 4,340,479, the polyamide resin is dissolved in a solvent, such as formic acid, and a non-solvent, such as water, is added under controlled conditions of agitation to achieve nucleation of the solution.

In inducing nucleation of the polyamide solution, a visible precipitate is formed which may partially or

completely redissolve. Preferably, any visible particles which do not redissolve should be filtered out of the system, e.g., with a 10 micrometer filter, prior to casting the nucleated solution or casting composition.

The nucleated solution or casting composition is then cast onto a substrate, e.g., a porous polyester sheet or web or a non-porous polyester sheet, in the form of a film and this film of solution is then contacted with and diluted by a liquid non-solvent system which is a mixture of solvent and a non-solvent for the polyamide resin. A preferred non-solvent liquid system for both the subject invention and that of U.S. Patent Specification No. 4,340,479 is a solution of water and formic acid. For the present invention, the formic acid is preferably present in an amount of from 35% to 60% by weight, all parts and percentages herein are by weight unless otherwise indicated. The polyamide resin thereupon precipitates from the solution, forming a hydrophilic membrane sheet on the substrate which can be washed to remove the solvent liquid. The membrane can then be stripped from the substrate and dried or, if the substrate is porous, it can be incorporated in the membrane to serve as a permanent support, in which event it is dried with the membrane. If the substrate is to

be incorporated into the membrane, it should be porous and capable of being wetted and impregnated by the casting composition, e.g., a porous, fibrous polyester sheet with an open structure. By appropriate control of process variables, membranes with through pores of uniform size and shape can be obtained. Conversely, if desired, tapered through pores, wider at one surface of the sheet and narrowing as they proceed towards the opposite surface of the sheet, can be obtained.

The same general procedure described above is followed in manufacturing the surface modified membranes of this previous invention except that the membrane surface modifying polymers used in the subject invention are combined with the solution of polyamide resin and the resulting modifying polymer/polyamide casting solution, after nucleation to form the cast composition, is cocast, resulting in unique membranes with novel properties extending the range of uses for microporous polyamide membranes.

The novel properties of membranes in accordance with United States Patent Specification 4,340,479 are believed to result in part from the high concentration on the exposed membrane surfaces of amine and carboxylic acid end groups of the polyamide. These amine and

carboxylic acid functions on the membrane surfaces result in unexpected membrane properties, such as their unusual zeta potential versus pH profile and their hydrophilic character.

It has now been discovered that the surface modified membranes in accordance with the present invention having unexpected and novel properties can be prepared using the general procedure disclosed in U.S. Patent Specification 4,340,479 but with the addition of low levels of selected membrane surface modifying polymers to the polyamide membrane casting solutions. Thus, surface modified, hydrophilic, microporous membranes with pore surfaces having a wide variety of desirable chemical and physical chemical properties are readily and economically prepared by the cocasting process in accordance with the present invention. These desirable membrane surface properties include, for example, negative zeta potential over a wide pH range. Such membranes have use in the enhanced filtration of positively-charged particulates, such as asbestos particles, through electrostatic capture. Useful surface modifying polymers for this purpose are polymers containing substantial proportions of acidic, ionizeable functional polar groups, such as carboxyl, sulfonic, phenolic amine, sulfhydryl, sulfide, thiocarbonyl,

phosphine, phosphoryl, thiophosphoryl or a non-reacting combination of any of these groups. These functional groups on the modified membrane surfaces provide negative zeta potential over a wide pH range, including acid media with pHs as low as 3, and enhanced filtration efficiency for positively charged particulates through electrostatic capture. Moreover, such surface modified membranes are also expected to show a reduced tendency for the adsorption of certain desirable components in pharmaceutical preparations.

Membranes prepared with selected surface modifying polymers have the ability to remove, selectively or universally, toxic and/or precious metals from aqueous fluids. Surface modifying polymers containing fuctional polar groups which undergo complex formation by interaction with metallic species by either ionic interaction or through complex forming interactions will produce bound metal species on the modified membrane surface. A variety of chemical functional groups are known to form stable metal complexes or metal salts and are therefore preferred functional membranes. These include amine, pyridyl, sulfonic, sulfhydryl, thiocarbonyl, phosphine, phosphoryl and imine, which are preferred because of their tendency to form stable complexes on salts with various metal species.

Membranes in accordance with the present invention having the ability to be further chemically modified for various purposes are those which have been prepared with surface modifying polymers bearing functional groups known to undergo further reactions efficiently and under relatively mild conditions. Preferred functional groups in this class include hydroxyl, carboxyl and amine. These groups, when occupying the surfaces of the membrane, can be further chemically reacted with, for example, enzymes, and serve as an efficient substrate for the immobilization of enzymes and other materials of interest.

Addition of as little as 1 weight percent (based on the polyamide resin) of the membrane surface modifying polymer to the membrane casting solution has been found to produce microporous hydrophilic membranes whose surface properties are substantially controlled by the surface modifying polymer. It is the ability of relatively small amounts of the membrane surface modifying polymer to control the surface properties of the membranes of the present invention which is believed to provide the desirable filtration characteristics and the desirable physiochemical surface behaviour of these membranes. The highly desirable properties of the

membranes of the subject invention are believed to result from the unique method of preparation in which the modifying polymer becomes an integral part of the overall structure of the membrane. As noted above, these desirable characteristics are obtained and controlled with a surprisingly low proportion of the membrane surface modifying polymer.

Membrane Surface Modifying Polymers:

The membrane surface modifying polymers or resins (sometimes hereinafter termed "modifying polymer(s)") useful in processes in accordance with this invention are those water-soluble polymers bearing the desired chemical functional groups and which are compatible with the polyamide membrane and soluble in the membrane casting solution. The preferred modifying polymers are those commercially available polymers which provide a high density of the desired functional group. The greater the number of desired functional groups per unit weight of modifying polymer, the greater is the extent to which the modifying polymer can impart the desired surface properties to the membrane.

Functional groups useful in membranes of this invention include hydroxyl, carboxyl, sulfonic, phenolic, amine,

sulfhydryl, sulfide, thiocarbonyl, phosphine, phosphoryl, thiophosphoryl, or a non-reacting (with each other) combination of any of the above groups. These functional groups are useful because (1) they are polar, (2) they have a high dipole moment, (3) they can participate in hydrogen bonding, either as donors, acceptors, or both, with materials of interest in the fluid medium, and (4) they can react in a conventional chemical sense and/or interact selectively with particulate material or dissolved material, or both, in the fluid medium. Because of their polarity and hydrogen bonding capability, these groups can interact strongly with the amine and carboxylic acid end groups of the polyamide from which the membrane is formed. While it is believed that this interaction occurs throughout the membrane structure, the nature of the membrane forming process is believed to cause preferential orientation of the modifying polymer toward the surfaces of the formed membrane. By this is meant that as a result of the cocasting process of this invenion, the modifying polymer determines the surface characteristics of the membrane. It is also believed that the interaction of the functional groups on the modifying polymer with the end groups of the polyamide results in intimate bonding of the modifying polymer and the polyamide resin forming an integral structure

thereby providing increased homogeneity of the pore surfaces of the membrane, and increased general stability, as evidenced by low levels of extractable matter, of the membranes produced by processes in accordance with this invention.

The modifying polymers have relatively high molecular weights. In principle, strong interaction between the modifying polymer and the polyamide resin would suggest that the stability of the membrane should be increased by inclusion of a modifying polymer. Surprisingly, it has been found that the inclusion of polymers of molecular weight less than 10,000 actually tend to produce membranes having unstable surface properties. For this reason, the modifying polymers in accordance with this invention have molecular weights of 10,000 or greater. Modifying polymers of molecular weight of 20,000 or greater tend to produce stable membranes and are preferred. A particularly preferred molecular weight range is from 25,000 to 150,000.

Surprisingly, the low added levels of modifying polymers appear to be preferentially orientated in such a manner as to result in membranes whose surface characteristics are substantially controlled by the membrane surface modifying polymer. This result is believed to reflect

both the unique membrane forming process and the hydrophilic nature of the modifying polymers. The combination of their hydrophilicity, their apparent strong interaction with the polyamide and groups and the unique membrane cocasting process is believed to result in the preferential orientation of the modifying polymers towards the membrane surface.

An additional, unexpected, and highly desirable characteristic of the membranes is that, while the surface modifying polymers are readily water-soluble, they are not leached out of the casting composition into the non-solvent liquid, typically water, which is used to precipitate the casting resin system. Apparently, the strong interaction of the modifying polymer with the polyamide end groups, coupled with the preferential orientation of the modifying polymer towards the membrane surface, perhaps under the influence of the non-solvent, combine to prove a membrane whose surface properties are substantially controlled by the functional polar groups of the modifying polymer. At any rate, the unexpected result is highly desirable, providing a membrane with unique characteristics which can be prepared by an efficient and economic process.

The modifying polymer of choice depends on the type of

chemical function desired at the surface of the membrane. This in turn, of course depends upon the desired use of the membrane.

Membranes with negative zeta potentials in the acidic pH range are made with highly anionic surface modifying polymers, such as those bearing a high concentration of carboxyl (COOH) or sulfonic (SO_3H) groups. Examples of materials containing such functional groups are poly(acrylic acid), poly(methacrylic acid), poly(styrene sulfonic acid) and copolymers of unsaturated carboxyl and sulfonic acids with non-ionic unsaturated monomers such as vinyl esters, acrylic esters, olefins and styrene.

Commercially available carboxyl-containing compositions are exemplified by the Carbopol (Registered Trade Mark) series of resins (B. F. Goodrich) described as high molecular weight polymers of acrylic acid. Copolymers containing carboxylic acids are exemplified by Gantrez S-97, a fully hydrolyzed copolymer of maleic anhydride with methyly vinyl ether and having a molecular weight of about 67,000. Product # 19205-8 (Aldrich Chemical Company) is a commercially available poly(acrylic acid) having a molecular weight of about 90,000. An example of a commercially available sulfonic acid-containing

polymer is Poly Sodium Vinyl Sulfonate (Air Products and Chemicals). A preferred modifying polymer for this invention is Versa TL-71 (National Starch), believed to be a homopolymer of styrene sulfonic acid having a molecular weight of about 70,000.

Membranes with amine functional groups may be prepared using modifying polymers bearing amino groups which are (1) pendent from the polymer backbone, (2) form part of the polymer backbone or (3) a combination thereof. In principal, any polymer containing amino groups may be used, such as polymers containing amino styrene or amino alkyl acrylates. Condensation products of alkylene dichlorides with alkylene diamines or ammonia, such as are sometimes used as flocculating agents, may also be useful, provided they have the desired molecular weight, solubility, and compatibility set forth earlier. Preferred are such materials as the polyethyleneimines, as exemplified by the Cor-Cat resins (Cordova Chemical Company), which are homopolymers of aziridine with molecular weights of 30,000 and greater, Cor-Cat P-145 being a particularly desirable example and having a molecular weight of 50,000 to 60,000.

Membranes with hydroxyl groups may be prepared using modifying polymers containing hydroxyl groups.

In principle, any polymer of high molecular weight with hydroxyl groups pendent from the polymer backbone can be used, such as polymers containing hydroxyaryl acrylates or hydroxyalkyl acrylates. However, poly (vinyl alcohol) is preferred because of its high density of hydroxyl groups. This polymer is commercially prepared by hydrolysis of poly (vinyl acetate) and is available as products having different degrees of hydrolysis, ranging from nearly 100 percent hydrolyzed to about 60 per cent hydrolyzed. Particularly preferred are compositions such as Vinol 165 (Air Products and Chemicals), a 99.6% hydrolyzed product of molecular weight of about 110,000.

Process Conditions

The preparation of the surface modified, skinless, hydrophilic, microporous, alcohol-insoluble polyamide membranes in accordance with this invention is carried out under controlled conditions including controlled addition of the non-solvent, e.g. water, to a solution of the polyamide and the membrane surface modifying polymer (casting solution), control of the concentration of the constitutents, control of the temperature and control of the agitation of the system to induce the

proper level of nucleation.

U.S. Patent Specification No. 4,340,479 includes a discussion therein concerning the relationship of the parameters set out above is generally applicable herein and will not be repeated. Rather, a summary of the operative ranges and their relationship will be provided.

Controlled Addition Of The Non-solvent:

The manner and rate of addition of the non-solvent to induce nucleation is interrelated with other process variables, such as intensity of mixing, temperature and the concentration of the various components of the casting solution. The term "casting solution" is used here to mean the solution made up of (A) the casting resin system and (B) the solvent system. Addition of the non-solvent is conveniently carried out through an orifice at a rate sufficient to produce a visible precipitate which, preferably, at least in part, subsequently redissolves. Maintaining all other parameters constant, casting compositions with quite different characteristics in terms of pore sizes of the resulting membranes will be obtained by varying the diameter of the orifice. The required degree of

nucleation resulting from non-solvent addition rate and orifice configuration is therefore best established by trial and error for each given system.

The controlled addition of non-solvent is discussed in detail in U.S. Patent Specification No. 4,340,479. Prior to addition of the non-solvent to induce nucleation, the casting solution is prepared. It is comprised of (a) an alcohol-insoluble polyamide resin as described above and (b) a membrane surface modifying polymer or resin and (B) a solvent system. The solvent system may simply be a solvent for the casting resin system, e.g. formic acid. Alternatively, the solvent system may contain an amount of a non-solvent, e.g. water. The amount of non-solvent present in the casting solution will always be less than the amount necessary to effect the stability of the solution.

Prior to casting, nucleation of the casting solution is initiated by the controlled addition of non-solvent liquid and agitation. The amount and rate of addition of non-solvent liquid is controlled along with the intensity of mixing or agitation. The advantage of including non-solvent as part of the solvent system in making up the casting solution, particularly in a continuous process, is that better control of the

addition of non-solvent can be maintained during the inducement of nucleation because smaller amounts of non-solvent are needed due to the non-solvent already present in the casting solution. As a result, better control of the addition rate can be maintained and a more uniform product of any desired pore size can be obtained.

Concentration Of The Constituents:

All parts and percentages herein are by weight unless otherwise stated.

The casting resin system is comprised of (a) an alcohol-insoluble polyamide resin having a methylene to amide ratio of from about 5:1 to about 7:1 and (b) a surface modifying polymer or resin as hereinbefore described.

The proportion of membrane surface modifying polymer to polyamide resin in the casting solution formed as the first step in the processes in accordance with this invention, based on the polyamide resin, can vary from as much as about 20 weight percent to as little as about 1.0 weight percent, that is, 20 parts of modifying polymer to 100 parts polyamide resin to 1 part of modifying polymer to 100 parts polyamide resin. The

generally preferred range of added modifying polymer is from about 5 weight percent to about 15 weight percent, based on the weight of the polyamide resin. For the purpose of membrane efficiency and production economy, the addition of about 5 weight percent of the modifying polymer, based on the polyamide resin, is particularly preferred. The polyamide resin is preferably present in the casting solution in an amount of from about 10% to 20%, and the surface modifying polymer will be present then in an amount of from about 0.5% to 3%, (based on all components present in the solution).

The amount of solvent present in the casting solution formed as the first step in processes in accordance with this invention will vary dependent upon the polyamide resin and the modifying polymer used. In general, the amount of solvent present will range from about 60 to 80% (based on all components present in the solution).

It should be understood that the casting solution comprises both (1) the casting resin system, i.e., the polyamide resin and the modifying polymer or resin, and (2) the solvent system, i.e., a solvent for the polyamide resin/modifying polymer casting resin system (such as formic acid) and, if desired, a minor amount of a non-solvent for the casting resin system (such as

water).

The amount of non-solvent, if any, present in the casting solution will in all cases be less than the amount in the liquid non-solvent system (membrane forming bath) used to precipitate the casting resin system from the casting composition, the casting composition being the composition formed from the initially prepared casting solution by inducing nucleation in that solution and, preferably, removing visible particles from the resulting composition. Generally, when the non-solvent is water, it will be present in the casting solution in an amount ranging from zero up to about 30% by weight, lesser amounts, such as 5-15%, being more desirable than the larger amounts (again based on all the components present in the solution).

Control Of The Temperature:

The temperature of the casting soltuion is not critical so long as it is maintained at a constant value. Generally, however, a decrease in casting solution temperature produces a higher degree of nucleation.

Control Of The Agitation

The intensity of mixing in a given system is a function of a large number of interrelated variables. For any given system, the mixing intensity can be expressed in terms of the rotation rate of the agitator. Such equipment has many forms and designs commonly used in the mixing art and is difficult to quantify. Thus, trial and error experimentation involving customary variables is necessary to establish the operable range of mixing intensities suitable for a particular system. Typically, using a 6.35 cm diameter ($2^1/_2$ inch) rotor operating at a throughput of about 500 to 1,500 grams of solution per minute requires mixing speeds in the range of from 1,500 to 4,000 RPM to produce membranes with pore ratings in the range of interest.

The liquid non-solvent system used to dilute the film of casting composition and thereby precipitate the casting resin system, typically by immersion in a bath of the liquid non-solvent system, can, and preferably does, contain a substantial amount of a solvent for the casting resin system, preferably the one present in the casting solution. That is, the liquid non-solvent system is comprised of a mixture of a non-solvent for

the casting resin system, e.g, water, and a solvent for the casting resin system, e.g., formic acid. However, on a percentage basis, the amount of solvent present in the liquid non-solvent system will be less than the amount present in the casting solution. Typically, the liquid non-solvent system will be comprised of a non-solvent, e.g., water, present in an amount ranging from about 65 to about 40 weight percent and a solvent for the casting resin system, e.g., formic acid, present in an amount ranging from about 35 to about 60 weight percent. Preferably, the bath of the liquid non-solvent system is maintained at a substantially constant composition with respect to non-solvent and solvent by the addition of non-solvent to the bath, preferably continuously, in a quantity sufficient to compensate for solvent diffusion into the bath from the thin film of casting composition.

Solvents

The solvent, comprising at least part, if not all, of the solvent system in the casting solution of the subject invention can be any solvent for the casting resin system. A preferred solvent is formic acid. Other suitable solvents are other liquid aliphatic acids, such as acetic acid and propionic acid; phenols, such as phenol; the cresols and their halogenated

derivatives; inorganic acids, such as hydrochloric, sulfuric and phosphoric; saturated aqueous or alcohol solutions of alcohol solutions of alcohol-soluble salts, such as calcium chloride, magnesium chloride and lithium chloride; and hydroxylic solvents, including halogenated alcohols.

The only criteria in selecting a solvent are that (1) it should form a solution of the polyamide resin and the modifying polymer, (2) it should not react chemically with either the polyamide resin or the surface modifying polymer and (3) it should be capable of ready removal from the surface modified polyamide membrane. Practical considerations also are important, of course. For example, inorganic acids are more hazardous to work with than are others of the named solvents and corrosion problems must be dealt with. Since formic acid meets the three criteria listed above and is a practical material as well, it is the solvent of choice. Due to economy and ease of handling, water is the non-solvent of choice for use in the solvent system when a non-solvent is used in the solvent system. In like manner, the preferred non-solvent added to the casting solution to induce nucleation thereof is water. The preferred non-solvent component of the liquid non-solvent system used to precipitate the casting resin system is also

water for the same reasons it is the non-solvent of choice in the solvent system.

The membrane products in accordance with this invention are characterized by being hydrophilic, skinless, microporous and alcohol-insoluble with narrow pore size distributions and pore sizes ranging from about 0.04 to about 10 micrometers; filtration efficiencies from molecular dimensions (pyrogens) up to particulates larger than the pore diameters; film thicknesses in the range of from about 0.01 to 1.5 millimeters, preferably from about 0.025 to about 0.8 mm; and, in the case of certain of the membranes, by a negative zeta potential in acidic media including pHs as low as 3. The membranes are hydrophilic, that is they are readily wettable by water, in less than 3 seconds, preferably less than 1 second.

The membranes are further characterized as having surface properties which are substantially controlled by functional polar groups of the modifying polymer which provides the membranes with the ability to selectively react or interact with (a) particulate matter in a fluid media, (b) dissolved matter in a fluid media, or (c) both (a) and (b). That is, it is believed that the process provides membranes in which a portion of the

functional polar groups of the modifying polymer react or interact with the surface carboxyl and amine end groups of the polyamide membrane to provide intimate bonding of the surface modifying polymer and the polyamide, but because the density of the surface chemical groups or functional polar groups in the surface modifying polymer is relatively high, functional polar groups remain available for reaction or interaction with one or more components of a fluid media. The excess functional polar groups contribute to the desired surface properties of the membrane. Indeed, the modifying polymer in any given membrane is chosen or tailored to fit the desired end use, e.g., a modifying polymer containing carboxyl or sulfonic acid groups may be chosenif a negative zeta potential in acidic media is desired.

The amount of surface modifying polymer and the density of the functional polar groups in the surface modifying polymer are chosen to provide an excess of the functional polar groups, that is, functional polar groups in excess of those reacting or interacting with the end groups of the polyamide. The excess of such groups on the pore surfaces of the membranes are available then as sites for further reaction or interaction. For example, these reactive sites can be

used to further modify the membrane with, e.g, bound enzymes. Other alternatives are to use these sites for (1) ion exchange mechanisms or (2) as the basis for dissolved metal entrapment by binding the metal at the reactive site on the membrane surface as a stable complex or coordination compound, (1) and (2) herein defined as "complex formation by interaction".

Surprisingly, the low added levels of the surface modifying polymers produce membranes whose surface characteristics substantially reflect the presence of the functional groups of the surface modifying polymers. Along with their excellent pore structure and, in certain cases, negative zeta potential in acidic media, these membranes have very low levels of extractable matter, making them particularly desirable for use in the filtration of biological and pharmaceutical preparations. Additionally, these membranes can be conveniently and economically prepared by a straightforward, continuous and clean process.

Method Of Testing The Surface Modified Membranes Of The Following Examples:

The zeta potentials of the membranes of the following examples were evaluated by the method described below:

Zeta Potential

The zeta potentials of the membranes were calculated from measurements of the streaming potential generated by flow of a 0.001 weight percent solution of KCl in distilled water through several layers of the membrane secured in a filter sheet or membrane holder. Zeta potential is a measure of the net immobile electric charge on a membrane surface exposed to a fluid. It is related to the streaming potential generated when the fluid flows through the membrane by the following formula (J. T. Davis et al, Interfacial Phenomena, Academic Press, New York, 1963):

$$\text{Zeta Potential} = \frac{4\pi\eta}{D} \quad \frac{E_s \lambda}{P}$$

where η is the viscosity of the flowing solution, D is its dielectric constant, λ is its conductivity, E_S is the streaming potential and P is the pressure drop across the membranes during the period of flow. In the following examples, the quantity $\frac{4\pi\eta}{D}$ was constant, having a value 2.052×10^2, or, when converted to kg./sq.cm., the constant must be multiplied by the conversion factor 703.1 so that the zeta potential can be expressed:

$$\text{Zeta Potential (mV)} = \frac{14.43 \cdot E_s \text{ (volts)} \cdot \lambda \text{ (}\mu\text{mho/cm)}}{P \text{ (kg/sq. cm.)}}$$

<u>General Method For The Preparation Of The Membranes Of Examples 1-5</u>

In the following examples, polyamide membranes were prepared containing a variety of membrane surface modifying polymers using the following general procedure:

Membrane casting solutions were prepared by dissolving nylon 66 resin pellets and the desired surface modifying polymer in a solution of formic acid. The nylon 66 resin used has a viscosity of about 6000 centipoise when tested at 30°C in a solution containing about 14.5 parts by weight of nylon 66, about 73 parts by weight formic acid and about 12.5 parts by weight water using a Rion Viscotester with a number 1 rotor (Model VT-04, available from Extech International Corp., Boston, Mass.) operating at 63.8 rpm. Dissolution took place with stirring at about 500 RPM in a jacketed resin kettle maintained at 30 degrees C.. When dissolution was complete (usually within 3 hours), a nonsolvent,

water, was added under controlled conditions of concentration, temperature, addition rate and degree of agitation to the casting solution in an amount sufficient to adjust the final concentration of materials to that given in each example and to form a casting composition. The water was pumped in, at the rate specified in each example through an orifice about 1 mm in diameter located under the surface of the solution and about 1 cm above a stirring blade mounted on a vertical shaft, to induce nucleation and form a visible precipitate. Stirring was maintained at about 500 RPM during addition of the water.

The casting composition was filtered through a 10 micrometer filter, after which about 40 grams of casting composition were spread out onto a clean glass plate by means of an adjustable gap doctor blade. The film was then promptly immersed into a bath containing formic acid and water in the amounts given in the examples below.

The membranes were kept immersed in the bath for several minutes to set them. They were then stripped from the glass plate, washed in water to remove residual formic acid and oven-dried for 15 minutes at 96 degrees C. (205 degrees F.) while restrained in a frame to prevent

shrinkage. The flat membrane sheets were then used for filter applications or for testing.

Example 1

The General Method described above was used to prepare a membrane where the surface modifying polymer was Cor-Cat P-145. The rate of injection of water was about 5 ml/min. The final casting composition solution contained about 73.7 weight percent formic acid, 9.9 weight percent water, 14.2 weight percent nylon 66 resin and 2.13 weight percent Cor-Cat P-145. The casting composition was drawn to a thickness of 0.017 inches on a glass plate and immersed in a bath containing 54 weight percent formic acid, the balance water. After the membrane was set, it was processed as described in the General Method until ready for testing.

The membrane produced was wetted completely immediately upon contact with water (in less than 1 second) and had a pore size of 0.8 micrometer as determined by K_L measurement. K_L measurements herein were determined using the technique disclosed in U.S. Patent Specification 4,340,479. The presence of functional groups of polyethyleneimine at the surface of the membrane was illustrated by the zeta potential of the

membrane, which was +10 mV at a pH of 8.0.

Example 2

The method of Example 1 was repeated, but with Product #19205-8 (Aldrich Chemical Company) as the surface modifying polymer. The rate of injection of water was 5 ml/min. The casting composition consisted of 74.8 weight percent formic acid, 10.1 weight percent water, 14.4 weight percent nylon 66 resin and 0.72 weight percent poly(acrylic acid). The casting composition was drawn to a thickness of 0.021 inch on a glass plate and immersed into a bath containing 50 weight percent formic acid, the balance water. After the membrane was set, it was further processed as described in the General Method until ready for testing.

The membrane produced was wetted completely immediately upon contact with water (in less than 1 second) and had a pore size of 8 micrometers as determined by K_L measurement. The membrane had a zeta potential of -4.0 mV at a pH of 3.6, a pH at which unmodified hydrophilic nylon membrane is strongly positive. This demonstrates that carboxylic acid functional groups of the surface modifying polymer are present at the surface of the

membrane and substantially control the surface characteristics thereof, even when the surface modifying polymer is added at this low level.

Example 3

The method of Example 1 was repeated, but with Versa TL-71 (National Starch Company) as the surface modifying polymer. The rate of injection of water was 2 ml/min. The casting composition contained about 74.2 weight percent formic acid, 12.9 weight percent water, 12.1 weight percent nylon 66 resin and 0.62 weight percent Versa TL-71. The casting composition was drawn to a thickness of 0.053 cm (0.021 inch) on a glass plate and immersed in a bath containing 50 weight per cent formic acid, the balance water. After the membrane was set, it was further processed as described in the General Method until ready for testing.

The membrane produced was wetted completely upon contact with water (in less than 1 second) and had a pore size of 0.2 micrometers as determined by K_L measurement. The membrane had a zeta potential of -2.4 mV at a pH of 3.6, a pH at which the unmodified nylon membrane is strongly positive, demonstrating that sulfonic acid groups of the modifying polymer are present at the surface of the

membrane and substantially control the surface characteristics thereof, even when the surface modifying polymer is added at this low level.

Example 4

The method of Example 1 was repeated, but with Gantrez S-97 (GAF Corporation) as the surface modifying polymer. The rate of water injection was 3 ml/min. The casting composition consisted of about 71.7 weight percent formic acid, 13.8 weight percent water, 13.8 weight percent nylon 66 resin and 0.70 weight percent Gantrez S-97. The casting composition was drawn to a thickness of 0.053 (0.021 inch) on a glass plate and immersed in a bath containing 50 weight percent formic acid, the balance water. After the membrane was set it was further processed as described in the General Method until ready for testing.

After drying, the membrane was wetted completely upon contact with water (in less than 1 second). It had a pore size of 0.8 micrometers as determined by K_L measurement and a zeta potential of -8.2 mV at a pH of 3.6, a pH at which unmodified hydrophilic nylon membrane is strongly positive, demonstrating that carboxylic acid functional groups of the Gantrez S-97 are present at the

surface of the membrane and substantially control the surface characteristics, even at the low levels at which the Gantrez S-97 was added.

Example 5

The method of Example 1 was repeated, but with Vinol 165 (Air Products) as the surface modifying polymer. The rate of water injection was 5 ml/min. The casting composition contained about 74.8 weight percent formic acid, 10.1 weight percent water, 14.4 weight percent nylon 66 resin and 0.73 weight percent Vinol 165. The casting composition was drawn to a thickness of 0.038 cm (0.015 inch) on a glass plate and immersed in a bath containing 50 weight percent formic acid, the balance water. After the membrane had set, it was processed further as described in the General Method until ready for testing.

The membrane produced was wetted completely on contact with water (in less than 1 second) and had a pore size of 1.0 micrometer as determined by K_L measurement.

A number of the membranes prepared in the previous examples were tested for the ability to remove metal ions from aqueous solution by complexation with the

functional groups of the modifying polymer on the membrane surface. The test was carried out by immersing 16 square centimeters of each membrane in 40 milliliters of a solution of 30 ppm Cu (as copper sulfate pentahydrate in deionized water) for 20 minutes. The copper ion concentration in the solutions, before and after exposure to the membranes, was established by the method described in <u>Standard Methods of Chemical Analysis</u>, N. H. Furman, Editor, Volume I, page 408, 6th Edition, Krieger Publishing Company, 1975, using tetramethylethylenediamine as the reagent. For comparative purposes, an unmodified hydrophilic nylon 66 membrane with a 0.2 micrometer pore size was included in the test evaluation. This membrane is listed as Control in Table I and has substantially no functional groups which are available for reaction with the copper ions.

TABLE I

Membrane of Example	Membrane Surface Functional Groups	Copper Adsorption Capacity in Milligrams per Square Meter Membrane Surface Area.
1	amine	95
2	carboxylic acid	130
3	sulfonic acid	605
5	hydroxyl	167
Control	none	30

The data in Table I demonstrate that the membranes in accordance with the present invention, prepared by the addition of certain surface modifying polymers, display surprisingly large metal adsorption capacities. The copper adsorption capacities observed with these membranes is believed to stem from the metal complex forming capability of the functional chemical surface groups in the membranes in accordance with the present invention. By constrast, the Control membrane, whose

surfaces have not been modified, displays low copper adsorption capacity. The microporous filtration membranes of the present invention have the novel capacity to function as fine filtration membranes with simultaneous removal of metal species from the filtering liquid through complex formation of the membrane surface functional groups with metal species. Such membranes are useful in the recovery of a variety of soluble or dispersed metal catalysts, in the metal detoxification of aqueous fluids and for various other similar applications.

The membrane of Example 1 was tested for its ability to undergo reaction with the dye Cibacron Blue F3G-A. Substrates modified with this dye have been found useful for the reversible binding or immobilization of certain enzymes, albumin, coagulation factors, and interferon (see Theory and Practice in Affinity Chromatography, P. V. Sundaram and F. Eckstein, Academic Press, New York, 1978, page 23-43). The membrane of Example 1 was immersed for 30 minutes at room temperature in a 0.2 weight percent aqueous solution of Cibacron Blue F3G-A (hereinafter referred to as Cibacron Blue), adjusted to a pH of 10 with sodium hydroxide. After exposure to the dye, the membrane was washed by agitation in distilled water until no blue color appeared to be lost in the

wash water. The membrane was then dried in an oven for one half hour at 107 degrees C. (225 degrees F.).

After the above treatment, the membrane of Example 1 had adsorbed a substantial quantity of Cibacron Blue, as evidenced by a deep blue membrane color. In order to demonstrate that all of the dye was firmly bound the membrane was next flushed with distilled water at a volume of 21.53 liters per square metre (2 liters per square foot of membrane area and then with a similar amount of a 0.01 M aqueous solution of tris (hydroxymethyl) aminomethane, (hereinafter referred to a "tris acetate") adjusted to pH 7.5 with acetic acid. This buffer ("tris acetate") and related buffers (e.g., "tris HCl") are commonly used in biochemical preparations and manipulations.

The membrane of Example 1 which had been dyed with Cibacron Blue was next evaluated as a support for affinity chromatography. A membrane suitable for affinity chromatography must bind firmly a substantial amount of enzyme, must retain this bound enzyme during washing with distilled water, and must release the bound enzyme on demand by treating with an appropriate substance, such as a substrate of the enzyme. To demonstrate such suitability, the dyed membrane of

Example 1 was next rinsed with 0.01 M tris acetate buffer adjusted to a pH of 7.5 in order to wet the membranes and establish the required pH. The membrane was then treated with the enzyme lactate dehydrogenase (Sigma Chemical Company L2500) by passing a solution containing 2.4 enzyme units/ml in the tris acetate buffer through the membrane at a total volume of 21.53 liters per square meter (2 liters per square foot) of membrane area. The quantity of enzyme bound by the membrane was determined by enzyme assay of aliquots of the enzyme solution before and after passage through the membrane. The amount of enzyme adsorbed to the exposed surfaces of the membrane was calculated by the measured differences in the enzyme concentration in the solution before and after passage through the membrane. Enzyme activity was assayed by observing the enzymatic conversion of NAD (nicontinamide adenine dinucleotide, oxidized form) into NADH (nicotinamide adenine dinucleotide, reduced form) by the standard method described in Sigman Chemical Company Technical Bulletin UV-200.

After the membrane was treated with the enzyme, it was flushed with 64.58 liters of distilled water per square metre (6 liters of distilled water per square foot) of membrane area over a period of about two

minutes so as to remove any enzyme which had not bound to the membrane. To demonstrate that bound enzyme was not subject to non-specific elution by distilled water, the flushed membrane was immersed in distilled water, about 3229 ml per square metre of membrane, (about 300 mil per square foot of membrane) for about 10 minutes. The distilled water was then analyzed for the presence of any released enzyme and was found to be substantially free of enzyme activity demonstrating that the enzyme was tightly bound to the membrane, as required. Biospecific elution of enzyme from the membrane surface was demonstrated by similar challenge with 0.004 M NAD in distilled water followed by analysis of the NAD solution for the present of the eluted enzyme. For comparative purposes, another sample of the surface modified membrane of Example 1 was subjected to the same sequence of treatments except that exposure to Cibacron Blue was omitted. This membrane is designated as Control in Table II.

TABLE II

Membrane of Example	Quantity of Enzyme Adsorbed in Enzyme Units Per Sq. Metre	Percent Bound Enzyme Eluted Non-Specific	Specific.
1	111,945 (10,400 per sq. ft)	2%	43%
Control	None	0	0

The results obtained with the membrane of Example 1 demonstrate that membranes in accordance with the present invention are useful as supports in affinity chromatography. The surface modified membrane of Example 1 binds high levels of Cibacron Blue chemically without the requirement of prior treatments. The membranes also bind Cibacron Blue in the required state since enzymes are bound in large quantities to the dyed membrane but not to undyed membranes. Moreover, the membrane bound enzyme is not subject to non-specific removal, such as, by treatment with water. However, the enzyme is removed specifically in a quantitative manner by the action of an appropriate enzyme substrate as required. Thus, membranes prepared by methods in accordance with this invention with selected surface

modifying polymers having certain functional polar groups are demonstrated to be suitable for applications in affinity chromatography.

Surface-modified membranes in accordance with this invention are also useful for other biotechnological applications. For example, the membrane of Example 1 has unexpected useful properties for the permanent chemical binding of enzymes on the membrane surface. To demonstrate permanent chemical binding of an active enzyme to the membrane surface, membrane of Example 1 was subjected to chemical treatments designed to allow such permanent chemical immobilization. The reactive chemical groups on the surface of the membrane of Example 1 were reacted with glutaraldehyde as a 25% solution in water by immersion of the membrane for 15 minutes at room temperature. Unbound glutaraldehyde was removed from the membranes by agitating twice for five minutes in aqueous solutions of 0.16 M sodium chloride.

Next, the chemical immobilization of the enzyme alkaline phosphatase was carried out. The glutaraldehyde-treated membrane was exposed for 15 minutes at room temperature to a solution of the enzyme alkaline phosphatase (Sigma Chemical Company, product P-7640). This solution contained 0.1 mg/ml of total protein dissolved in 0.16 M

aqueous NaCl, and had an enzymatic activity of about 0.4 enzyme units/ml as determined by standard procedures (Sigma Technical Bulletin 104). Exposure to the enzyme permitted the membrane surface-bound glutaraldehyde to react with and irreversibly bind the enzyme onto the membrane surface.

Any enzyme which was loosely adsorbed to the membrane but not chemically bound was removed by agitating membranes for three successive two minute periods in solutions containing 0.01 M tris acetate, buffer at pH 7.5, in 0.16 M aqueous NaCl. To ensure complete removal of unreacted enzyme the membranes were then exhaustively washed with a surfactant solution containing 0.1% Triton X-100 (Rohm & Haas Co., an adduct of nonylphenol with about 10 moles of ethylene oxide) in water. Finally, the surfactant was removed by two successive washes with the tris acetate buffer solution. As a control, a hydrophilic nylon membrane of similar pores size but prepared without the addition of surface-modifying polymer was subjected to the same sequence of treatments in an attempt to similarly immobilize enzyme.

The membrane of Example 1 and the Control were then tested for the presence of active, immobilized enzyme. The presence of membrane-bound enzyme was detected by

exposing membranes to a solution of p-nitrophenyl phosphate, a substrate for the enzyme, and observing the characteristic change in the color of the solution caused by the reaction of the substrate with the enzyme. Thus, a 10 x 10 mm piece of each membrane was exposed for approximately one-half hour to a 5 ml aliquot of solution containing 0.001 M p-nitrophenylphosphate in 0.1 M aqueous "tris" buffer adjusted to pH 9 with HCl. The presence of membrane surface bound enzymne activity was easily detected by the formation of a brilliant yellow color, due to the action of the enzyme on the substrate. The level of enzyme activity was measured by visual color comparison with standard solutions containing known concentrations of the dissolved enzyme. As shown by the data in Table III, the membrane of Example 1 shows a high level of enzyme activity indicating the chemical binding of enzyme by the functional groups of the surface modified membrane of this invention. In contrast, the Control membrane prepared without added membrane surface modifying polymer did not chemically bind enzyme as shown by the complete absence of enzyme activity.

TABLE III

Membrane of Example	Measured Enzyme Activity in Enzyme Units Per Square Metre Membrane Area
1	269.1 (25 units per square foot)
Control	less than 0.1

These results illustrate several important and surprising points. First, it is demonstrated that surface-modified membranes in accordance with the present invention can be used as supports for the chemical immobilization of enzymes. The results clearly demonstrate that enzymes can be permanently attached to the membrane surface in large quantities. Moreover, the immobilized enzyme has been demonstrated to be permanently bound to the membrane surface and yet to retain high enzymatic activity. Furthermore, the method of immobilization described above will be recognized by those skilled in the art as (1) exposing the enzyme to only a very mild or benign treatment and (2) providing a very simple, clean and fast process requiring no prior membrane surface preparation.

Industrial Applicability :

Surface modified membranes in accordance with the present invention have been demonstrated to be superior in many important filtration related properties to prior art membranes. They can be used for filtering applications in their manufactured form, with or without the incorporation of the substrate upon which they are formed. Two or more membranes can be combined or secured to each other to form multiple layer membrane filter sheets or they may be converted into filter elements by known methods and employed in filter cartridges, e.g., as filter elements in the form of a corrugated sheet supported within a conventional cartridge.

Certain of membranes in accordance with this invention display negative zeta potentials in acidic media including at a pH as low as 3. Accordingly, these membranes show greatly enhanced removal efficiencies toward positively charged particles in acidic media. Furthermore, they have enhanced efficiency to selectively remove particulate matter from fluid media, to remove undesired dissolved material from fluid media, to concentrate desirable dissolved material, to be chemically modified as required to be useful for

processing biological and biochemical preparations and they can serve as substrates for the immobilization of enzymes.

These membranes have uses in industry, particularly in the pharmaceutical, medical and biochemical fields, for treatment of various fluid media. These include treatment of waste streams for the recovery of valuable metals, the immobilization of enzymes, and generally for any use where an ion containing fluid must be filtered to a high degree of clarity.

CLAIMS

1. A process for preparing a surface modified, skinless, hydrophilic, microporous, alcohol-insoluble polyamide membrane with controlled pore surface properties, capable of reacting or interacting in a controlled manner with (a) particulate matter in a fluid, (b) non-particulate matter in a fluid, or (c) both (a) and (b) and that is readily wetted by water, which process is characterized by the steps of ;

(1) preparing a casting solution comprising (A) a casting resin system including (a) an alcohol-insoluble polyamide resin having a ratio CH_2 :NHCO of methylene CH_2 to amide NHCO groups within the range of from 5:1 to 7:1 and (b) a water-soluble, membrane surface modifying polymer having functional polar groups and a molecular weight of 10,000 or greater, and (B) a solvent system in which said casting resin system is soluble;

(2) inducing nucleation of said casting solution by controlled addition of non-solvent for said casting resin system under controlled conditions of concentration, temperature, addition rate and degree of agitation to obtain a visible precipitate of casting resin system particles, thereby forming a casting composition;

(3) spreading said casting composition on a substrate to form a thin film thereof on the substrate;

(4) contacting and diluting the film of said casting composition with a liquid non-solvent system for said casting resin system comprising a mixture of solvent and non-solvent liquids, thereby precipitating said casting resin system from said casting composition in the form of a thin, skinless, hydrophilic, surface modified, microporous, polyamide membrane with controlled pore surface properties;

(5) washing said membrane to remove solvent; and

(6) drying said membrane.

2. A process according to claim 1 characterized in that the precipitated casting resin system particles are redissolved or are filtered out before spreading said casting compositions on said substrate.

3. A process according to claim 1 or claim 2 characterized in that the polyamide resin is polyhexamethylene adipamide, poly-e-caprolactam, or polyhexamethylene sebacamide.

4. A process according to claim 1, characterized in that said polyamide resin is polyhexamethylene adipamide, said solvent system for said casting resin system comprises formic acid, and said non-solvent added to induce nucleation is water.

5. A process according to any of claims 1 to 4 characterized in that the film of casting composition is contacted with said liquid non-solvent system by immersing said film carried on said substrate in a bath of said liquid non-solvent system.

6. A process according to any of claims 1 to 5 characterized in that said membrane surface modifying polymer contains functional polar groups of hydroxyl, carboxyl, sulfonic, phenolic, amine, sulfhydryl, sulfide, thiocarbonyl, phosphine, phosphoryl, thiophosphoryl or a non-reacting combination thereof.

7. A process according to any one of claims 1 to 6 characterized in that said casting composition is continuously spread onto said substrate, said thin film of said casting composition is continuously immersed in a bath of said liquid non-solvent system, and the bath is maintained at a substantially constant composition with respect to non-solvent and solvent by the addition of non-solvent

to the bath in a quantity sufficient to compensate for solvent diffusion into the bath from said thin film of said casting composition.

8. A process according to claim 7 characterized in that the substrate is a fibrous polyester sheet or other porous web having an open structure which is wetted and impregnated by the casting composition, thereby forming a membrane film of having the porous web incorporated as a part thereof.

9. A surface modified, skinless, hydrophilic, microporous, alcohol-insoluble, polyamide membrane characterized in that it is derived from an alcohol-insoluble hydrophobic polyamide resin having a ratio CH_2 :NHCO of methylene CH_2 to amide NHCO groups within the range of from 5:1 to 7:1, said membrane having (1) the surface properties thereof substantially controlled by a membrane surface modifying polymer having functional polar groups and a molecular weight of 10,000 or greater, and (2) having the capability of reacting or interacting in a controlled manner with (a) particulate matter in a fluid, (b) non-particulate matter in a fluid, or (c) both (a) and (b).

10. A membrane according to claim 9 characterized in that the surface properties thereof are substantially controlled by the functional polar groups of a surface modifying polymer having functional polar groups and comprising hydroxyl, carboxyl, sulfonic, phenolic, amine, sulfhydryl, thiocarbonyl, phosphine, phosphoryl, thiophosphoryl, or a non-reacting combination thereof.

11. A membrane according to claim 9 or claim 10 characterized in that surface thereof have the ability to undergo complex formation by interaction of functional polar groups on said surfaces with metallic species in a fluid media.

12. A membrane according to claim 11 characterized in that said functional polar groups are amine, pyridyl, sulfonic, sulfhydryl, thiocarbonyl, phosphine, phosporyl, and imine.

13. A filter element comprising a surface modified, skinless, hydrophilic, microporous, alcohol-insoluble polyamide membrane according to any one of claims 10 to 12.

14. An integral surface modified, skinless, hydrophilic, microporous, alcohol-insoluble polyamide membrane characterized in that it is derived from an 80 to 99.9% of an alcohol-insoluble hydrophobic polyamide resin having a ratio CH_2 :NHCO of methylene CH_2 to amide NHCO groups within the range of from 5:1 to 7:1, and from 20 to 0.1% of a membrane surface modifying polymer having functional polar groups and a molecular weight of 10,000 or greater, said membrane having (1) the surface properties thereof substantially controlled by functional polar groups of the membrane surface modifying polymer and (2) having the capability of reacting or interactingin a controlled manner with (a) particulate matter in a fluid (b) non-particulate matter in a fluid, or (c) both (a) and (b).

European Patent Office

EUROPEAN SEARCH REPORT

0087228
Application number

EP 83 30 0517

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl. 3)
A	US-A-4 244 817 (H. YAGINUMA) * Claim 1, column 2, line 49 *	1,8	B 01 D 13/04
A	EP-A-0 031 730 (TEIJIN) * Claims 1, 4 *	1,6	
P,A	EP-A-0 056 175 (TEIJIN) * Claim 1 *	1	
A	EP-A-0 005 536 (PALL) * Claims 1, 2, 5-7, 10, 12 *	1-5,7, 8	
D,P A	US-A-4 340 479 (D.B. PALL) * Claims 1-3, 5-10, 155-158 *	1-5,7- 9	
A	DE-A-2 457 355 (RHONE-POULENC) * Claims 6, 7 *	6	

TECHNICAL FIELDS SEARCHED (Int. Cl. 3)

B 01 D 13/04
C 08 J 5/22
C 08 J 5/24
C 08 J 9/40
C 08 J 9/42

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
BERLIN	20-05-1983	KUEHN P

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO Form 1503. 03.82